

AD No. 15527
ASTIA FILE COPY

Technical Report for Project Entitled
ORIENTATION STUDIES IN REACTIONS ACCOMPANIED BY
NEIGHBORING GROUP EFFECTS

Contract Nonr-85200 - Task NR 055-316

Summary of First Year
1 June 1952 - 1 June 1953

ad 15527

Department of Chemistry, University of Kansas
Lawrence, Kansas

By C. A. VanderWerf and C. A. Stewart

NEIGHBORING GROUP EFFECTS

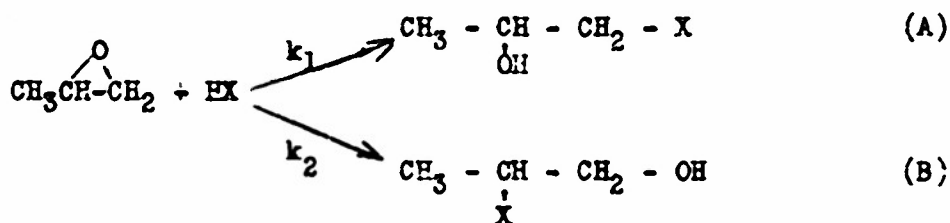
Contract Nonr-85200-Task NR 056-316

I. Summary of Work of First Twelve Months.

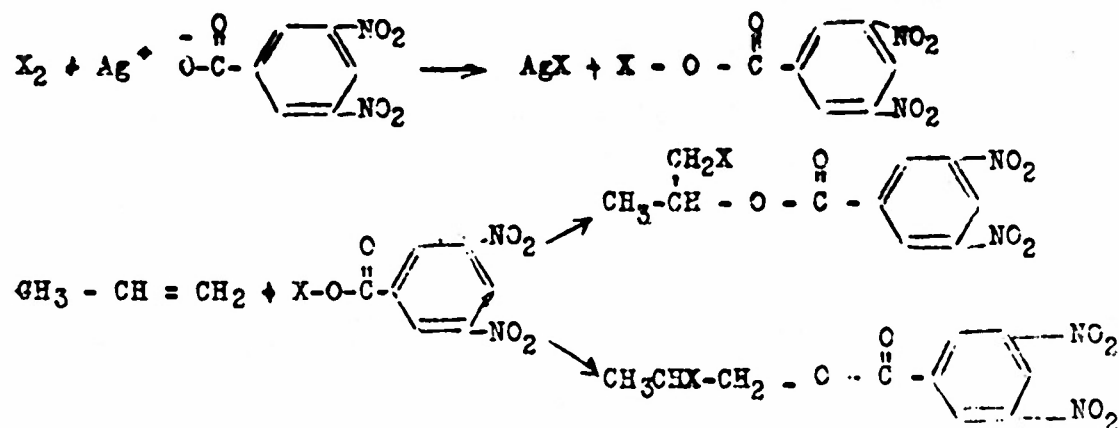
- A) Preparation of Compounds. The propylene chloro-, bromo-, and iodohydrins obtainable from reaction of propylene with the respective hydrohalic acids have been prepared in pure state and have been adequately characterized by physical properties, including infrared spectra, and by preparation of their 3,5-dinitrobenzoates, which are crystalline solids.
- B) Analytical Procedures. Suitable analytical procedures have been developed for each of the above pairs of isomers, and semi-quantitative analysis of the dinitrobenzoates has also been accomplished. These analytical procedures involve infrared spectrophotometry and are based upon comparison of spectra of unknown mixtures with the spectra of the pure isomers and of synthetic mixtures.

Before the development of the infrared method, considerable effort was expended in attempts to devise suitable analytical methods based upon fractional distillation or upon the solubility of benzoic acid in mixtures of the two isomers. Neither of these methods had been satisfactorily developed at the time the infrared method became available, and both were abandoned in favor of the more rapid and reliable infrared technique.

- C) Ring Opening Reactions of Propylene Oxide. The reaction of propylene oxide with hydrohalic acids has been studied under varying conditions of temperature, solvent, and catalyst. The relative percentages of the two isomeric products A and B obtained under different conditions have been explained on a theoretical basis.



D) Addition of Positive Halogen Salts. A study has been made of the reaction

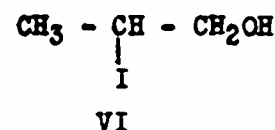
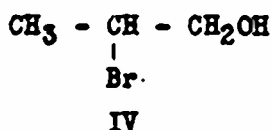
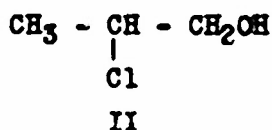
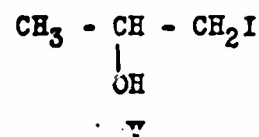
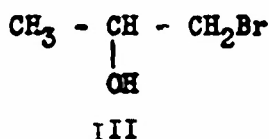
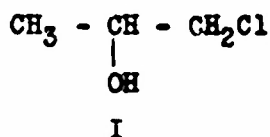


where X is chlorine, bromine, or iodine, in two different solvents and at two different temperatures. The results may be explained in terms of an intermediate carbonium ion, or, when X = bromine or iodine, in terms of the cyclic "halonium" ion proposed by Halperin, Donahoe, Kleinberg, and VanderWerf (1) for an analogous reaction.

E) Publication of Data. In addition to this report, and previous status reports, the experimental results of this investigation are included in the Doctoral Dissertation of C.A. Stewart (2), and an article is being prepared for submission to the Journal of the American Chemical Society.

II. Experimental Results.

A) Preparation and Properties of Compounds. The preparation and properties of 1-chloro-2-propanol (I), 2-chloro-1-propanol, (II), 1-bromo-2-propanol (III), and 2-bromo-1-propanol (IV) have been described in previous reports. 1-Iodo-2-propanol (V) and 2-iodo-1-propanol (VI) have been prepared in 86 and 67% yields respectively, by refluxing of the corresponding bromohydrins, III and IV, with a slight excess of sodium iodide in acetone for ten and



forty hours, respectively. The physical properties of V and VI are listed in Table I.

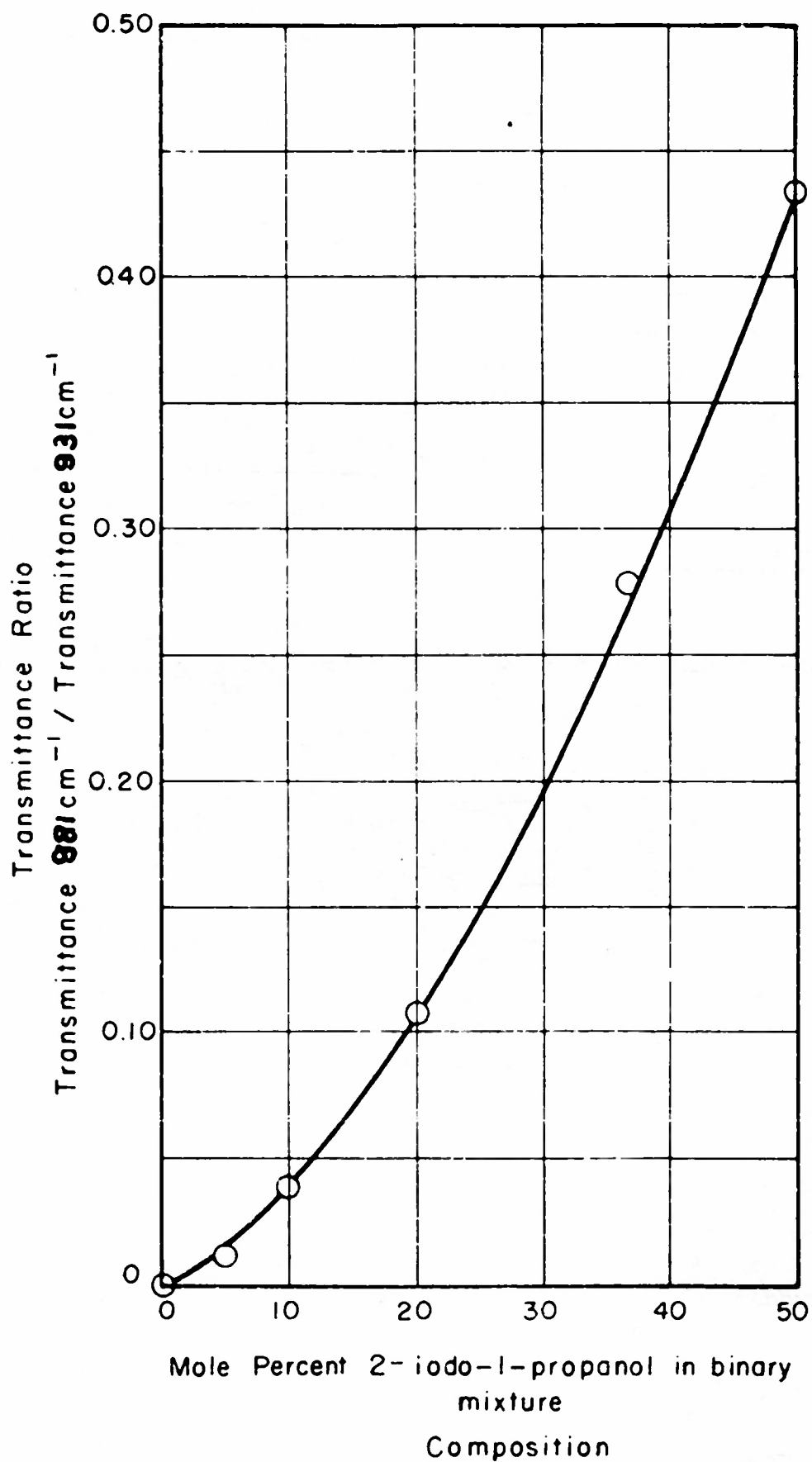
TABLE I
Physical Properties of 1-Iodo-2-propanol (V) and
of 2-Iodo-1-propanol (VI)

	V	VI
Boiling Point	59-63°/9mm.	62-66°/9mm.
Refractive Index, n_D^{30}	1.5365	1.5392
Density, 30°	1.8999	1.8902
Molar Refraction	30.54	30.33 (calc., 30.37)
Neutralization Equivalent	185.2	181.5 (calc., 186.0)
Melting Point of 3,5-Dinitrobenzoate	80.6-83.8	99.4-100.5
Frequency of Peak Used for Infrared Analysis	931 cm^{-1}	981 cm^{-1}

Satisfactory elemental analyses were obtained for all of the 3,5-dinitrobenzoates.

B) Analytical Procedures. Mixtures of the iodohydrins were analyzed in the same manner as the chlorohydrins and bromohydrins. Infrared spectra of the pure isomers and of the synthetic mixtures were determined in 0.025 mm. salt cells on a Perkin-Elmer Model 21 Infrared Spectrophotometer. The heights of the two peaks which differed in the two isomers were measured in percent transmission from the minimum between them, and the ratio of these two heights plotted against composition. Unknown mixtures were analyzed by determination of the spectra in the same manner and reading of the compositions corresponding to the observed heights ratio from the graph. The dinitrobenzoates obtained were analyzed by visual comparison of the spectra in the range 800 to 1200 cm^{-1} with spectra of the pure isomers, and of synthetic mixtures.

~~Figure 11~~ Calibration Curves for Infrared Analysis
of 1-iodo-2-propanol and 2-iodo-1-propanol



C) Ring Opening of Propylene Oxide. Propylene oxide was treated with hydrogen chloride, with hydrogen bromide, and with hydrogen iodide under the following conditions: (a) Propylene oxide was added slowly to (1) a solution 2.5 N with respect to NaCl and 6N with respect to hydrochloric acid, (2) concentrated hydrobromic acid, and (3) 1:1 concentrated hydriodic acid; (b) propylene oxide was added slowly to ether (or acetone in one case) containing a trace of thymol blue, while anhydrous hydrogen chloride or bromide was passed in at such a rate as to maintain the solution at the yellow-pink color change of the indicator (pH 2-3 in water); (c) propylene oxide was added slowly at reflux temperature to a solution of magnesium bromide etherate; (d) propylene oxide was added to a solution 7N in ammonium bromide, and hydrobromic acid was added at such a rate as to maintain the solution at the color change of methyl orange (pH 4-5); (e) propylene oxide was added to a solution 7N in sodium bromide, and 40% aqueous acetic acid was added at such a rate as to maintain the pH at 7-9.

The products were distilled (after extraction and drying in the case of the aqueous reactions) through a Vigreux column; this operation was shown to produce no change in isomeric composition. The properties and compositions of the products so obtained are given in table II.

TABLE II
Ring Opening Reactions of Propylene Oxide

Reagent	Solvent and Procedure	Temp., °C	Yield, %	Neutralization Equivalent *	% I, III or V	% II, IV or VI
HCl	Ether (b)	-55	96	94.5	89	11
	"	-27	89	95.0	87	13
	"	12	87	95.9	80	20
	"	35	85	95.5	74	26
	Water (a)	15	40	94.9	62	38
	"	33	64	94.8	63	37
	"	60	64	95.0	62	38
	"	83	54	95.5	57	43
	Acetone (b)	10	87	94.8	84	16
HBr	Ether (b)	-45	98	#	92	8
	"	15	100	#	85	15
	Water (a)	15	77	138.4	76	24
	"	35	84	138.4	74	26
	"	55	77	139.0	72	28
	"	75	76	139.7	71	29
AgBr ₂	Ether (c)	35	60	139.3	84	16
NH ₄ Br	Water (d)	30	71	---	77	23
NaBr	Water (e)	22	43	139.2	95	5
HI	Water (a)	-10	75	"	88	12
	"	65	75	"	82	18

* Calculated, C₃H₇OCl, 94.5; C₃H₇OBr, 139.0

Impure products (C₃H₆Br₂ or iodine present).

D) Addition of Positive Halogen Salts. To 0.05 mole of silver 3,5-dinitrobenzoate in 200 ml. of anhydrous solvent (0.025 mole per 100 ml. of solvent) the theoretical quantity (or a slight excess) of halogen was added. After a shaking period of a few minutes, propylene was bubbled in until no further reaction occurred. At dry ice temperature, in ether, only the secondary ester was obtained, in agreement with the results of Kalperin, Donahoe, Kleinberg, and VanderWerf (1). At zero degrees, however, 10% of the isomeric product was obtained when the reaction was carried out in ether, and 25% when it was carried out in chloroform, either with or without the addition of catalytic amounts of dibenzoyl peroxide.

III. Discussion of Results

A. Synthesis and Analysis. The synthetic method employed in the preparation of the chloro- and bromohydrins are in agreement with earlier investigations which have shown the usefulness of lithium aluminum hydride in such syntheses. The preparation of pure iodohydrin isomers by sodium iodide exchange on the halohydrins is new in its application to this field, and it is interesting that no isomerization takes place during the reaction. Dewael (3) in an analogous reaction found that both 1-chloro-2-propanol and 2-chloro-1-propanol reacted with potassium cyanide to give 3-hydroxy-butyronitrile. Since no neighboring group effect is observed with iodide, it is likely that Dewael's results were due to intermediate formation of the epoxide by the basic cyanide ion, with subsequent addition of hydrogen cyanide to the epoxide.

The infrared method of analysis is of inestimable value in problems of this type. It is rapid and convenient and should be generally applicable to the isomeric mixtures obtained in this field of study. It requires only that pure isomers be available for calibration.

B. Ring Opening Reactions of Propylene Oxide. According to the absolute reaction rate theory, following the derivation of Hammett (4), the relative rates of two reactions, or in this case, the relative amounts of the two isomeric products, should be related to the entropies and enthalpies of activation by the equation:

$$\ln \frac{(A)}{(B)} = \ln \frac{k_1}{k_2} = \frac{\Delta S^\ddagger_1 - \Delta S^\ddagger_2}{R} - \frac{\Delta H^\ddagger_1 - \Delta H^\ddagger_2}{RT}$$

where (A) and (B) are the relative amounts of products, k_1 and k_2 the rate constants, ΔS^\ddagger_1 and ΔS^\ddagger_2 the entropies of activation, ΔH^\ddagger_1 and ΔH^\ddagger_2 the enthalpies of activation, R the ideal gas constant, and T the absolute temperature. From this equation, a plot of the logarithmic ratio

of products against reciprocal temperature should give a straight line whose slope is proportional to the enthalpy term, and whose intercept ("infinite temperature value") should be proportional to the entropy difference. The experimental data are plotted in Figures I and II, and the entropy and enthalpy differences so calculated are given in Table III.

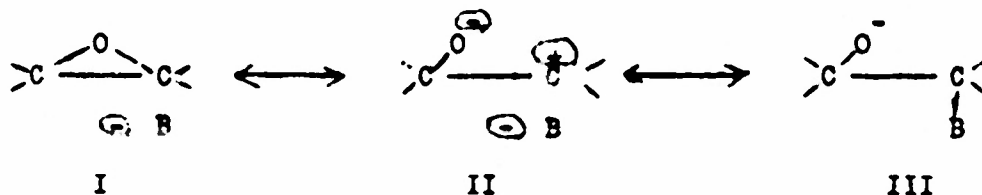
TABLE III
Differences in Entropy and Enthalpy of Activation

Series	Halide	Solvent	$\Delta^{\ddagger}S^{\ddagger}$, cal/mole	$\Delta^{\ddagger}H^{\ddagger}$, kcal/mole
(1)	Cl	Water	-0.85	-0.55
(2)	Br	"	-0.70	-0.85
(3)	I	"	-0.32	-1.12
(4)	Cl	Ether	-2.8	-1.54
(5)	Br	"	-2.0	-1.56

(A) and k_1 are for reaction of the halogen at the terminal carbon,
(B) and k_2 for reaction at the secondary carbon.

The entropy differences are consistent with the picture of steric hindrance. As the attacking base becomes larger, steric hindrance becomes larger, and the entropy difference should become more positive, as is observed for the order chloride < bromide < iodide.

The enthalpy differences may be explained in terms of the transition state theory. The transition state for the reaction may be considered a resonance hybrid of three structures:



The effect of substitution will be determined largely by structure II, since hyperconjugative or inductive stabilization of the positive charge on carbon is possible in this structure. As the strength of the attacking base increases, structure III should become increasingly important; hence, structure

II will become less important, and the effect of resonance on orientation will decrease. In the series chloride, bromide, and iodide, the base strength as given by the Swain correlation (5) increases, and the enthalpy term increasingly favors primary, rather than secondary attack.

The effect of the solvent is hard to rationalize. Perhaps, in water, where reactants are more highly solvated, the energy required for activation is greater; then the reaction will have more carbonium ion character, and a higher percentage of secondary attack should be expected.

The fact that basic conditions are more favorable to primary attack than are acid conditions, as shown in the case of bromide ion, is also in agreement with resonance considerations. Acid catalysis should give greater carbonium ion character to the transition state, by weakening the carbon-oxygen bonds and by decreasing the amount of charge separation in the resonance structure (II) corresponding to carbonium configuration. Due to the increased contribution of structure II, one should expect more secondary attack with the acid catalysis. Magnesium bromide etherate and ammonium bromide gave essentially the same results as did hydrogen bromide; since Swain (5) has shown that the ring opening of epoxides is subject to general acid catalysis, these results seem consistent with a mechanism in which ammonium ion or magnesium complexes act as acid catalysts.

- C. The Addition of Positive Halogen Salts to 1-Propene. Although the results obtained might be adequately explained in terms of an open carbonium ion, the data are also explainable on the basis of the cyclic ion proposed as an intermediate in such reactions,



By formal analogy with the ring opening of epoxides, if it is assumed that the "halonium" ion has greater carbonium ion character than the

transition state in even the acid catalyzed epoxide reactions (corresponding to a greater contribution of structure II in the transition state) then more secondary attack is to be expected for the halonium ion. The previously observed direction of solvent effect is noted here, also; ether, which is a more basic solvent than chloroform and hence is better able to solvate the positive halogen salt, gives a greater amount of secondary attack.

IV. Suggestions for Future Work.

The materials are now available for the investigation of such reactions as the conversion of the halohydrins to mixed dihalides by reaction with thionyl chloride or phosphorus halides, and the conversion of halohydrins to hydroxy esters by reaction with silver and sodium salts of organic acids in order to determine whether or not neighboring group effects are operative and in order to ascertain the orientation in reactions involving neighboring group effects. In addition, the background has been laid and analytical methods have been developed for a study of such reactions of propylene as the addition of hypohalous acids and of halogens in the presence of a high concentration of other anion, such as the salt of an organic acid.

B. Bibliography

- (1) B. I. Halperin, H.B. Donahoe, J. Kleinberg, and C.A. VanderWerf, *J. Org. Chem.*, 17, 623 (1952).
- (2) C. A. Stewart, Ph.D. Thesis, University of Kansas, 1953.
- (3) A. Dewael, *Bull. soc. chim. Belg.*, 3, 504 (1924).
- (4) L. P. Hammett, *Physical Organic Chemistry*, McGraw-Hill, New York, 1940 pp.118-124.
- (5) C. G. Swain, *J. Am. Chem. Soc.*, 73, 2813 (1951); *ibid*, 75, 136 (1953).

Figure ~~III~~ I

Van't Hoff Plot, Propylene Oxide + HX, Aqueous

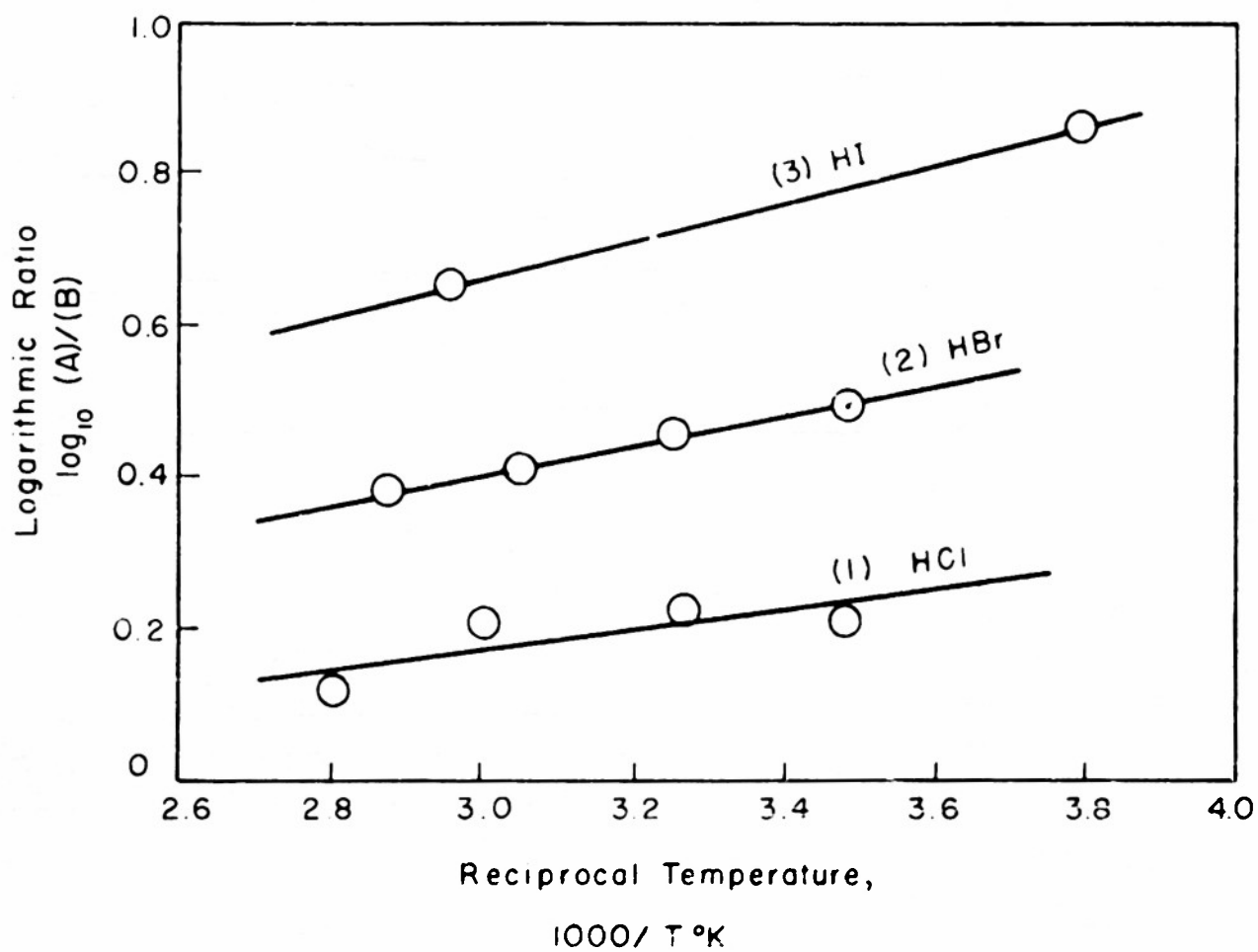


Figure ~~IV~~ II

Van't Hoff Plot, Propylene Oxide + HX, Ether

